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Particulate matter and SARS-CoV-2: A possible model of COVID-19 transmission

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ABSTRACT

Coronavirus disease 2019 (COVID-19), an acute respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly developed into a pandemic throughout the world. This disease is a highly infectious novel coronavirus and can affect people of all ages. Previous reports observed that particulate matter (PM) provided a platform for intermixing with viruses (i.e., influenza). However, the role of PM in SARS-CoV-2 transmission remains unclear. In this paper, we propose that PM plays a direct role as a “carrier” of SARS-CoV-2. SARS-CoV-2 is reported to have a high affinity for the angiotensin-converting enzyme 2 (ACE2) receptor. Indirectly, exposure to PM increases ACE2 expression in the lungs which facilitates SARS-CoV-2 viral adhesion. Thus, the high risk of SARS-CoV-2 in heavily polluted regions can be explained by upregulation of ACE2 caused by PM. PM could be both a direct and indirect transmission model for SARS-CoV-2 infection.

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1. Introduction

Coronavirus disease 2019 (COVID-19), an acute respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly developed into a pandemic throughout the world. A cluster of patients with unknown pneumonia was reported in late December 2019 in Wuhan, China (Zhu et al., 2020a). As of 12 July 2020, according to the World Health Organization (WHO),

COVID-19 had resulted in 12,552,765 confirmed cases and 561,617 reported deaths worldwide. It is known that this is a coronavirus, relatively similar to the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) coronaviruses (Lu et al., 2020). The highly contagious COVID-19 can infect people of all ages (Sanche et al., 2020); however, transmission models of SARS-CoV-2 via particulate matter (PM) remain unclear.

2. PM and COVID-19

The effect of meteorological factors in association with the atmospheric pollution on the spread of PM and virus infection was considered in previous studies. Carducci et al. (2013) found that different virus types were detected in various kinds of temperature and humidity. Recently, several reports in Europe, China, and the USA investigated

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associations between PM and COVID-19 (Frontera et al., 2020a; Sciomer et al., 2020). Specifically, a study on migrant workers and refugees postulated that biomass smoke from cooking and heating could increase the risk of COVID-19 (Thakur et al., 2020). A study involving 120 cities in China showed that a $10 \mu\text{g}/\text{m}^3$ increase in PM of $<2.5 \mu\text{m}$ in aerodynamic diameter ($\text{PM}_{2.5}$) led to more than a 2% increase in new COVID-19 cases (Zhu et al., 2020b). However, it was argued that this rise in COVID-19 infection was related to the high population density rather than the short-term exposure to air pollution (Copiello and Grillenzoni, 2020). PM_{10} and $\text{PM}_{2.5}$ were found to be associated with the COVID-19 incidence in Xiaogan, China (Li et al., 2020). A recent report indicated that Lombardi and Emilia Romagna in northern Italy had higher COVID-19 mortality levels compared to other regions of Italy (Conticini et al., 2020). Notably, these regions are also among the most heavily polluted due to the high density of factories, heavy traffic volumes, and its specific topography of being surrounded by mountains which prevents air cycling (Frontera et al., 2020b). Another study also found that northern Italy, which is polluted with high levels of PM_{10} and $\text{PM}_{2.5}$, was highly affected by COVID-19 (Martelletti and Martelletti, 2020). Fattorini and Regoli (2020) observed a significant correlation between chronic exposure to PM_{10} and $\text{PM}_{2.5}$ and COVID-19 cases in northern Italy. Zoran et al. (2020) found an association of PM_{10} and $\text{PM}_{2.5}$ with new confirmed COVID-19 cases. A study conducted in California (USA) found a significant association of PM_{10} and $\text{PM}_{2.5}$ with COVID-19 mortality (Bashir et al., 2020). In a cross-sectional study involving 98% of the American population, an increase in $1 \mu\text{g}/\text{m}^3$ in $\text{PM}_{2.5}$ exposure resulted in nearly a 10% increase in COVID-19 mortality (Wu et al., 2020). Epidemiological evidence suggests that PM could be a risk factor for COVID-19. However, the role of PM in the COVID-19 transmission is poorly understood.

3. PM containing SARS-CoV-2 RNA: the role of direct transmission

Aerosols containing SARS-CoV-2 RNA were detected in a hospital in Wuhan, China (Liu et al., 2020). However, the role of outdoor PM on COVID-19 transmission remains unclear. Recently, Setti et al. (2020a, 2020b) used a polymerase chain reaction (PCR) approach to detect SARS-CoV-2 RNA on 34 PM_{10} samples collected from Bergamo, Italy during the COVID-19 pandemic outbreak, which saw its first confirmed case on January 31st 2020. They found gene E in 15 samples and the RdRP gene, which is highly specific to SARS-CoV-2, in four samples. These data suggest that SARS-CoV-2 RNA can be found in ambient PM_{10} in urban regions. Similar evidence for the influenza virus was previously reported. Viable avian influenza viral RNA was found in PM up to 60 m downwind of commercial turkey farms using reverse-transcription (RT)-PCR and culture techniques (Jonges et al., 2015). Influenza viral RNA was detected in air samples collected approximately 2 km from the farms (Corzo et al., 2013). A study in the US reported that PM_{10} had higher estimated concentrations of avian influenza virus than $\text{PM}_{2.5}$, but $\text{PM}_{2.5}$ may be further aerally transported (Zhao et al., 2019). That paper also reported transmission of the avian influenza virus via $\text{PM}_{2.5}$ within a state and between states (Zhao et al., 2019). Viruses may be adsorbed through coagulation onto PM and remain airborne for hours or days (Martelletti and Martelletti, 2020), thereby increasing inhaled concentrations of virus via PM in the lungs. In brief, $\text{PM}_{2.5}$ may provide a good platform to “shade” and “carry” the SARS-CoV-2 during atmospheric transport. Thus, PM containing SARS-CoV-2 could be a direct transmission model in a highly polluted area.

4. Upregulation of angiotensin-converting enzyme 2 (ACE2) by PM exposure in the lungs: the role of indirect transmission

COVID-19 respiratory illness is caused by the SARS-CoV-2 positive-sense single-stranded RNA virus (Yang and Wang, 2020). The lungs are the primary target for SARS-CoV-2 infection by droplet-aerosol transmission, especially in respiratory zones. The size of SARS-CoV-2

ranges between ~70 to 90 nm as observed by transmission electron microscopy, and it is present in a wide range of intracellular organelles (i.e., vesicles) after infection of cells (Kim et al., 2020). ACE2 is the main entrance for SARS-CoV-2 infection (Hoffmann et al., 2020). The spike glycoprotein of SARS-CoV-2 has a higher affinity for ACE2 in host cell targets (Vankadari and Wilce, 2020; Wrapp et al., 2020); therefore, ACE2 receptors provide an adhesion site for SARS-CoV-2 to invade cells (Brake et al., 2020). A recent report indicated that ACE2 is predominantly expressed in a transient secretory cell type in the subsegmental bronchial branches of the lungs (Lukassen et al., 2020). Our previous study found that 3 months of exposure to PM_{10} increased ACE2 expression in rat lungs (Chuang et al., 2020). Exposure to cigarette smoke up-regulated ACE2 expression, thus providing adhesion sites for SARS-CoV-2 (Brake et al., 2020). Particle effects on ACE2 were also found in a previous study. ACE2-knockdown mice showed increased pulmonary phosphorylated (p)-signal transducer and activator of transcription 3 (STAT3) and p-extracellular signal-regulated kinase 1/2 (ERK1/2) levels after fine particle-induced acute lung injury (Lin et al., 2018). Aztatzi-Aguilar et al. (2015) exposed rats to different sizes of PM during 3 days and 8 weeks, and found that ACE2 messenger (m)RNA was higher in the treatment group than in the control group, which suggested elevated expression of ACE2 protein in the lungs. In another study, mice treated with $\text{PM}_{2.5}$ showed a significant increase in ACE2 in the lung 2 and 5 days after instillation (Lin et al., 2018). Upregulation of ACE2 by PM_{10} was also observed in human alveolar A549 and human respiratory epithelial cells (Miyashita et al., 2020). In conclusion, exposure to PM increases the expression of ACE2 allowing for SARS-CoV-2 adhesion. Thus, PM-upregulated ACE2 could be an indirect transmission model for SARS-CoV-2 infection.

5. Conclusions

SARS-CoV-2 transmission is a crucial public health concern, and many aspects of this route urgently require further study. Currently, increasing evidence has shown that droplet-aerosol transmission is an important route for SARS-CoV-2 infection. Epidemiological reports identified an association between PM and COVID-19; however, the underlying mechanisms remain unclear. In this paper, we hypothesized that PM is a possible transmission model for COVID-19 by direct and/or indirect SARS-CoV-2 infection of the lungs. First, $\text{PM}_{2.5}$ may provide a good platform to “shade” and “carry” the SARS-CoV-2 during atmospheric transport. Thus, $\text{PM}_{2.5}$ containing SARS-CoV-2 could be a direct transmission model in a highly polluted area. Second, PM upregulates ACE2 expression and SARS-CoV-2 has high affinity for the ACE2 receptor. This suggests that PM may increase the risk of SARS-CoV-2 via ACE2 expression. The combination of PM and SARS-CoV-2 may aggravate lung injury by increasing inflammation. Herein, providing insights into the risk of airborne transmission of SARS-CoV-2 via PM.

Authors' contributions

All authors contributed substantially to the concept and design of the study, drafting of the article, and critically revising the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript for publication.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Aztatzti-Aguilar, O.G., Uribe-Ramirez, M., Arias-Montano, J.A., Barbier, O., De Vizcaya-Ruiz, A., 2015. Acute and subchronic exposure to air particulate matter induces expression of angiotensin and bradykinin-related genes in the lungs and heart: angiotensin-II type-I receptor as a molecular target of particulate matter exposure. *Part Fibre Toxicol* 12, 17.
- Bashir, M.F., Ma, B.J., Bilal Komal, B., Bashir, M.A., Farooq, T.H., et al., 2020. Correlation between environmental pollution indicators and COVID-19 pandemic: a brief study in Californian context. *Environ. Res.* 187, 109652.
- Brake, S.J., Barnsley, K., Lu, W., McAlinden, K.D., Eapen, M.S., Sohal, S.S., 2020. Smoking Upregulates angiotensin-converting Enzyme-2 receptor: a potential adhesion site for novel coronavirus SARS-CoV-2 (Covid-19). *J. Clin. Med.* 9, 841.
- Carducci, A., Federigi, I., Verani, M., 2013. Virus occupational exposure in solid waste processing facilities. *Ann Occup Hyg* 57, 1115–1127.
- Chuang, H.-C., Chen, Y.-Y., Hsiao, T.-C., Chou, H.-C., Kuo, H.-P., Feng, P.-H., et al., 2020. Alteration in angiotensin-converting enzyme 2 by PM1 during the development of emphysema in rats. *ERJ Open Research*.
- Coticini, E., Frediani, B., Caro, D., 2020. Can atmospheric pollution be considered a co-factor in extremely high level of SARS-CoV-2 lethality in northern Italy? *Environ. Pollut.* 261, 114465.
- Copiello, S., Grillenzoni, C., 2020. The spread of 2019-nCoV in China was primarily driven by population density. Comment on “association between short-term exposure to air pollution and COVID-19 infection: evidence from China” by Zhu et al. *Sci. Total Environ.* 744, 141028.
- Corzo, C.A., Culhane, M., Dee, S., Morrison, R.B., Torremorell, M., 2013. Airborne detection and quantification of swine influenza A virus in air samples collected inside, outside and downwind from swine barns. *PLoS One* 8, e71444.
- Fattorini, D., Regoli, F., 2020. Role of the chronic air pollution levels in the Covid-19 outbreak risk in Italy. *Environ. Pollut.* 264, 114732.
- Frontera, A., Cianfanelli, L., Vlachos, K., Landoni, G., Cremona, G., 2020a. Severe air pollution links to higher mortality in COVID-19 patients: the “double-hit” hypothesis. *J. Inf. Secur.* 264, 114732.
- Frontera, A., Martin, C., Vlachos, K., Sgubin, G., 2020b. Regional air pollution persistence links to COVID-19 infection zoning. *J. Inf. Secur.* 81 (2), 318–356.
- Hoffmann, M., Kleine-Weber, H., Schroeder, S., Kruger, N., Herrler, T., Erichsen, S., et al., 2020. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 181 (2), 271–280.
- Jonges, M., van Leuken, J., Wouters, I., Koch, G., Meijer, A., Koopmans, M., 2015. Wind-mediated spread of low-pathogenic avian influenza virus into the environment during outbreaks at commercial poultry farms. *PLoS One* 10, e0125401.
- Kim, J.M., Chung, Y.S., Jo, H.J., Lee, N.J., Kim, M.S., Woo, S.H., et al., 2020. Identification of coronavirus isolated from a patient in Korea with COVID-19. *Osong Public Health Res Perspect* 11, 3–7.
- Li, H., Xu, X.L., Dai, D.W., Huang, Z.Y., Ma, Z., Guan, Y.J., 2020. Air pollution and temperature are associated with increased COVID-19 incidence: a time series study. *Int. J. Infect. Dis.* 97, 278–282.
- Lin, C.I., Tsai, C.H., Sun, Y.L., Hsieh, W.Y., Lin, Y.C., Chen, C.Y., et al., 2018. Instillation of particulate matter 2.5 induced acute lung injury and attenuated the injury recovery in ACE2 knockout mice. *Int. J. Biol. Sci.* 14, 253–265.
- Liu, Y., Ning, Z., Chen, Y., Guo, M., Liu, Y., Gali, N.K., et al., 2020. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. *Nature* 582, 557–560.
- Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., et al., 2020. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 395, 565–574.
- Lukassen, S., Lorenz Chua, R., Trefzer, T., Kahn, N.C., Schneider, M.A., Muley, T., et al., 2020. SARS-CoV-2 receptor ACE2 and TMPRSS2 are primarily expressed in bronchial transient secretory cells. *EMBO J.* 39 (10), e105114.
- Martelletti, L., Martelletti, P., 2020. Air pollution and the novel Covid-19 disease: a putative disease risk factor. *SN Compr Clin Med* 1–5.
- Miyashita, L., Foley, G., Semple, S., Grigg, J., 2020. Traffic-Derived Particulate Matter and Angiotensin-Converting Enzyme 2 Expression in Human Airway Epithelial Cells. *bioRxiv.* (2020.05.15.097501).
- Sanche, S., Lin, Y.T., Xu, C., Romero-Severson, E., Hengartner, N., Ke, R., 2020. High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. *Emerg. Infect. Dis.* 26.
- Sciomer, S., Moscucci, F., Magri, D., Badagliacca, R., Piccirillo, G., Agostoni, P., 2020. SARS-CoV-2 spread in northern Italy: what about the pollution role? *Environ. Monit. Assess.* 192, 325.
- Setti, L., Passarini, F., De Gennaro, G., Barbieri, P., Pallavicini, A., Ruscio, M., et al., 2020a. Searching for SARS-COV-2 on particulate matter: a possible early Indicator of COVID-19 epidemic recurrence. *Int. J. Environ. Res. Public Health* 17.
- Setti, L., Passarini, F., De Gennaro, G., Barbieri, P., Perrone, M.G., Borelli, M., et al., 2020b. SARS-Cov-2RNA found on particulate matter of Bergamo in northern Italy: first evidence. *Environ. Res.* 188, 109754.
- Thakur, M., Boudewijns, E.A., Babu, G.R., van Schayck, O.C.P., 2020. Biomass use and COVID-19: a novel concern. *Environ. Res.* 186, 109586.
- Vankadari, N., Wilce, J.A., 2020. Emerging WuHan (COVID-19) coronavirus: glycan shield and structure prediction of spike glycoprotein and its interaction with human CD26. *Emerg Microbes Infect* 9, 601–604.
- Wrapp, D., Wang, N., Corbett, K.S., Goldsmith, J.A., Hsieh, C.L., Abiona, O., et al., 2020. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science* 367, 1260–1263.
- Wu, X., Nethery, R.C., Sabath, B.M., Braun, D., Dominici, F., 2020. Exposure to Air Pollution and COVID-19 Mortality in the United States: A Nationwide Cross-Sectional Study. *medRxiv.* (2020.04.05.20054502).
- Yang, P., Wang, X., 2020. COVID-19: a new challenge for human beings. *Cell Mol Immunol* 17, 555–557.
- Zhao, Y., Richardson, B., Takle, E., Chai, L., Schmitt, D., Xin, H., 2019. Airborne transmission may have played a role in the spread of 2015 highly pathogenic avian influenza outbreaks in the United States. *Sci. Rep.* 9, 11755.
- Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al., 2020a. A novel coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.* 382, 727–733.
- Zhu, Y., Xie, J., Huang, F., Cao, L., 2020b. Association between short-term exposure to air pollution and COVID-19 infection: evidence from China. *Sci. Total Environ.* 727, 138704.
- Zoran, M.A., Savastru, R.S., Savastru, D.M., Tautan, M.N., 2020. Assessing the relationship between surface levels of PM2.5 and PM10 particulate matter impact on COVID-19 in Milan, Italy. *Sci. Total Environ.* 738, 139825.